REMARKS

The Present Invention

The present invention pertains to a recombinant expression vector, a host cell comprising the same, a method for detecting a nucleic acid encoding Rig, and a method for amplifying a nucleic acid encoding Rig.

The Pending Claims

Claims 1-4 and 6-16 are pending of which claims 1-3 are directed to a recombinant expression vector, claim 4 is directed to a host cell comprising the same, claims 6-10 are directed to a method of detecting a nucleic acid encoding Rig, and claims 11-16 are directed to a method of amplifying a nucleic acid encoding Rig.

The Office Action

The Office has objected to the specification for allegedly containing embedded hyperlinks and/or other form of browser-executable code. The Office has objected to claims 11-16 for allegedly reciting the acronym "PCR." The Office also has alleged that the application fails to comply with the requirements of 37 C.F.R. 1.821-1.825 in that Figure 2 and the specification contain sequences that are not labeled with SEQ ID NO: tags. The Office has rejected claims 6-16 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement and written description. The Office has also rejected claims 1-4 and 6-16 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Office has rejected claims 1 and 4 under 35 U.S.C. § 102 (b) as allegedly anticipated by Lamerdin et al., GenBank Accession No. AC006538 (herein referred to as Lamerdin et al.). Claims 6-15 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Yu et al., *P.N.A.S.* 96: 214-219 (1999) (herein referred to as Yu et al.). Claims 1 and 2 have been rejected under 35 U.S.C. § 103 (a) as allegedly *prima facie* obvious in view of Lamerdin et al. The Office has rejected claims 1, 3 and 4 under 35 U.S.C. § 103 (a) as allegedly obvious in view of Lamerdin et al., Kimmelman et al., *Oncogene* 15: 2675-2685 (1997) (herein referred to as Kimmelman et al.), U.S. Patent No. 6,077,686 (herein referred to as the '686 patent), and Baker et al., *Nucleic Acids Res.* 25: 1950-1956 (1997) (herein referred to as Baker et al.). Claims 1, 6-11 and 13-15 have been rejected under § 103 (a) as allegedly obvious in view of Lamerdin et al. in combination with Kimmelman et al. Claim 12 has been rejected under § 103 (a) as allegedly obvious in view of Lamerdin et al. in combination with Kimmelman, U.S. Patent No. 4,695,188 (herein

referred to as the '188 patent), and U.S. Patent No. 5,981,183 (herein referred to as the '183 patent). The Office also rejects claim 15 under 35 U.S.C. § 103 (a) as allegedly obvious in view of Lamerdin et al. in combination with Kimmelman et al. and the '188 patent. Claim 16 has been rejected under 35 U.S.C. § 103 (a) as allegedly obvious in view of Lamerdin et al. in combination with Kimmelman et al., U.S. Patent No. 5,314,809 (herein referred to as the '809 patent), and U.S. Patent No. 5,397,703 (herein referred to as the '703 patent). Reconsideration of these objections and rejections is hereby requested.

Amendments to the Specification and the Claims

The specification has been amended to delete any embedded hyperlinks and/or other form of browser-executable code. Claim 1 has been amended to recite "A recombinant expression vector consisting essentially of an open reading frame operably linked to one or more regulatory elements, wherein the open reading frame encodes a protein having the amino acid sequence of SEQ ID NO: 5" and is supported in the specification at, for instance, page 23, line 13 through page 28, line 28. In view of the changes made to claim 1, claim 2 has been amended to recite "said open reading frame has" in lieu of "said nucleotide sequence is." Claim 3 has been amended to recite "is" in lieu of "further comprises." Claim 6 has been amended to recite "A method for detecting a nucleic acid," "a sample comprising a nucleic acid encoding Rig," "a nucleic acid probe," and "whereupon the detection of the hybridization complex indicates the presence of a nucleic acid encoding Rig in the sample." Claims 8 and 14 have been amended to recite "is from" in lieu of "comprises." Claim 10 has been amended to recite "hybridization complex in step c) is detected using" in lieu of "method comprises." Claim 11 has been amended to recite the definition of the acronym "PCR" followed by the acronym in parentheses. Claim 11 has also been amended to recite "A method for amplifying a nucleic acid encoding Rig," "two oligonucleotides, one of which is complementary to the nucleotide sequence of SEQ ID NO:4 and one of which is complementary to the nucleotide sequence that is complementary to SEQ ID NO: 4," and "whereupon a nucleic acid encoding a Rig is amplified," wherein the latter phrase replaces the phrase "to produce an amplified product; and." Claim 11 has further been amended to delete step e), which is now the subject matter of newly added claim 29. Claim 16 has been amended to recite "wherein one of said two oligonucleotides consists of SEQ ID NO: 2 and the other of said two oligonucleotides consists of SEQ ID NO: 3." No new matter has been added by way of these amendments. Claims 5 and 17-28 have been cancelled as drawn to a non-elected invention. Applicants reserve the right to

pursue any cancelled subject matter in a continuation, continuation-in-part, divisional, or other application. Cancellation of any subject matter should not be construed as abandonment of that subject matter.

Drawing Amendments

The Examiner is requested to approve the accompanying replacement drawings. Figures 1 and 2 have been amended to identify all nucleotide and amino acid sequences with appropriate SEQ ID NO:s.

Discussion of the Claim Objections

The Office has objected to claim 11 for allegedly using the acronym "PCR" without having it defined in the first instance of use in the claims. Claim 11 has been amended to recite "polymerase chain reaction (PCR)." In view of this amendment, the objection is believed to be moot.

Discussion of the Indefiniteness Rejection

The Office has rejected claims 1-4 and 6-16 under Section 112, second paragraph, as allegedly indefinite. Specifically, the Office contends that it is unclear what is intended by the term "Rig." This rejection is traversed as the specification is replete with guidance as to what is meant by the term "Rig." For instance, the specification at page 4, lines 27 and 28, teaches that Rig stands for "Ras-related Inhibitor Gene" and that the Rig protein is a member of the Ras protein family and has tumor suppressing activity. The specification further teaches the Rig amino acid sequence (SEQ ID NO: 5) and a cDNA sequence encoding the Rig protein (SEQ ID NO: 4). Further taught by the specification is the tissue expression pattern of Rig (Figure 4), the tumor expression pattern of Rig (Figure 5), the focus formation inhibiting activity of Rig (Figures 6 and 8), the ability of Rig to bind to Raf-1 (Figure 9), and the ability of Rig to inhibit tumor growth (Figure 10). Given all of these teachings of the Rig protein, one of ordinary skill in the art would be able to make a determination as to what is and is not a Rig protein.

In view of the foregoing, one of ordinary skill in the art can determine the metes and bounds of the pending claims. Therefore, Applicants request that the rejection under Section 112, second paragraph, be withdrawn.

Discussion of the Lack of Written Description Rejection

The Office has rejected claims 6-16 under 35 U.S.C. 112, first paragraph, as allegedly lacking a written description. This rejection is traversed for the reasons set forth below.

The Office specifically contends that the scope of the claims is unclear, as a minimum requirement for Rig polypeptides is not set forth in the specification. The Office further argues that it is unclear as to whether or not the 8 Ras-related polypeptides disclosed in the specification are considered Rig polypeptides. However, as discussed above, one of ordinary skill in the art is able to make a determination as to what is and is not a Rig protein, given all of the teachings on the Rig protein in the specification. The minimum functional requirements are those characteristics of Rig that are described in the specification, e.g., tumor growth inhibiting activity, focus formation inhibiting activity, and ability to bind to Raf-1. The structural requirements of a Rig polypeptide, as one of ordinary skill in the art recognizes after reading the specification in its entirety, are those amino acid sequences having high identity with SEQ ID NO: 5, wherein the encoded protein functions according to a Rig protein. Furthermore, Figures 2 and 3 make it clear that the other Ras-related polypeptides are not considered Rig polypeptides, since the specification at page 8, lines 7 and 8, discloses that Figure 2 is an alignment of the Rig amino acid sequence with the amino acid sequences of *other* human Ras-family members and Figure 3 demonstrates the divergent evolution of the different Ras-related genes. That Rig is on its own branch of this evolutionary any tree makes it clear to one of ordinary skill in the art that the other Ras family members are not considered to be Rig polypeptides. Therefore, a Rig protein is adequately described, such that the scope of the pending claims is discernible by one of ordinary skill in the art.

In view of the foregoing, the subject invention is, in fact, adequately described in the specification. Therefore, Applicants request that the rejection for lack of written description be withdrawn.

Discussion of the Lack of Enablement Rejection

The Office has rejected claims 6-16 under Section 112, first paragraph, as allegedly lacking enablement. This rejection is traversed for the reasons set forth below.

The Office specifically contends that the specification is not enabling for methods of detecting or amplifying a nucleic acid encoding a Rig polypeptide other than the nucleic acid having the nucleotide sequence of SEQ ID NO: 5, namely because the term "Rig polypeptide" renders the scope of the claims unclear. However, as discussed above,

one of ordinary skill in the art is able to make a determination as to what is and is not a Rig protein, given all of the teachings on the Rig protein in the specification. Furthermore, one of ordinary skill in the art is enabled to test a given nucleic acid molecule to see if it encodes a Rig polypeptide.

The specification, moreover, teaches how to detect a nucleic acid encoding a Rig polypeptide at, for instance, page 45, line 6, through page 46, line 18, and page 79, line 17, through page 80, line 15, and teaches how to amplify a nucleic acid encoding a Rig polypeptide at, for example, page 17, line 15, through page 18, line 27, and page 78, lines 7-19. For nucleic acids encoding a Rig polypeptide other than the nucleic acid having the nucleotide sequence of SEQ ID NO: 5, the steps of the inventive methods would be the same as those described herein, except that the nucleotide sequence of the probes might be different, depending on where in the nucleotide sequence the nucleic acid having a sequence other than SEQ ID NO: 5 differed with respect to SEQ ID NO: 5. One of ordinary skill in the art, in view of the teachings of the instant specification, is equipped with the knowledge to design primers that would anneal to a nucleic acid encoding a Rig polypeptide having a nucleotide sequence other than SEQ ID NO: 5.

The Office has also rejected claims 11-16 as allegedly lacking enablement, since the claims are directed to a method of amplifying nucleic acids encoding Rig with two oligonucleotide probes, both of which have complementarity to the nucleotide sequence of SEQ ID NO: 4. Applicants assert that this was an inadvertent error. Claim 11 has been amended to correct this error by amending the claim to recite "two oligonucleotides, one of which is complementary to the nucleotide sequence of SEQ ID NO:4 and one of which is complementary to the nucleotide sequence that is complementary to SEQ ID NO: 4" and is supported in the specification at, for instance, page 17, lines 25 and 26. In view of this amendment, this rejection is believed to be moot.

In view of the foregoing, one of ordinary skill in the art is enabled to make and/or use the subject invention. Therefore, Applicants request that the lack of enablement rejections be withdrawn.

Discussion of the Anticipation Rejection

The Office has rejected claims 1 and 4 under Section 102 (b) as allegedly anticipated by GenBank Accession No. AC006538. The Office has also rejected claims 6-15 under Section 102 (b) as allegedly anticipated by Yu et al. These rejections are traversed for the reasons set forth below.

The Office specifically contends that GenBank Accession No. AC006538 discloses a bacterial artificial chromosome (BAC) comprising 177 kb of human chromosome 19, including a segment encoding the amino acid sequence of SEQ ID NO: 5 and 105 kb of upstream genomic sequence. The Office concludes that "it is clear that this nucleic acid comprises the transcriptional control elements for this open reading frame. For this reason, the bacterial artificial chromosome...is an expression vector for SEQ ID NO: 5" (see page 14 of Paper No.13). However, as one of ordinary skill in the art recognizes, a BAC is a high-capacity vector for *replication* of the sequences contained within the BAC, not for *expression* of these sequences (see Sambrook et al., Molecular Cloning: A Laboratory Manual, 3rd ed., Cold Spring Harbor Press, Cold Spring Harbor, N.Y., pages 4.1-4.4, (2001), which is attached hereto). From the teachings of the specification and the knowledge in the art, it is clear that the BAC of GenBank Accession No. AC006538 is not a *recombinant expression vector* and, thus, does not fall within the scope of either of claims 1 or 4.

However, in order to advance prosecution and not in acquiescence of the rejection, claim 1 has been amended to recite "A recombinant expression vector consisting essentially of an open reading frame operably linked to one or more regulatory elements, wherein the open reading frame encodes a protein having the amino acid sequence of SEQ ID NO: 5" and is supported in the specification at, for instance, page 23, line 13, through page 28, line 28. In view of this amendment, this rejection is believed to be moot.

The Office further alleges that Yu et al. discloses detection of a poly mRNA from human tumor tissue of a nucleic acid encoding Noey2, a polypeptide that is 63% identical to SEQ ID NO: 5. The Office further asserts that Yu et al. discloses identification of a Noey2 gene in genomic DNA. The Office concludes that, because the specification allegedly does not exclude Noey2 from the genus of polypeptides that may be construed as a Rig polypeptide, Yu et al. anticipates a method of detecting nucleic acids encoding Rig in a sample. However, as stated above, from the teachings of the specification, e.g., Figures 2 and 3, it is clear to one of ordinary skill in the art that a Noey2 polypeptide is not a Rig polypeptide. Therefore, Yu et al. does not anticipate the present inventive methods of detecting nucleic acids encoding Rig.

In view of the foregoing, the subject invention is not anticipated by the prior art. Therefore, Applicants hereby request that the rejections under Section 102 (b) be withdrawn.

Discussion of the Obviousness Rejections

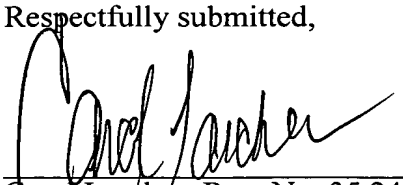
The Office has rejected claims 1 and 2 under Section 103 (a) as allegedly *prima facie* obvious in view of GenBank Accession AC006538. The Office also has rejected claims 1, 3, and 4 under Section 103 (a) as allegedly *prima facie* obvious in view of GenBank Accession No. AC006538 in combination with Kimmelman et al., the '686 patent; and Baker et al. Claims 1, 6-11, and 13-15 also have been rejected under Section 103 (a) as allegedly *prima facie* obvious in view of GenBank Accession No. 006538 in combination with Kimmelman et al. Claim 12 has been rejected under Section 103 (a) as allegedly *prima facie* obvious in view of GenBank Accession No. AC006538 in combination with Kimmelman et al. and the '188 and '183 patents. Claim 15 also has been rejected under Section 103 (a) as allegedly *prima facie* obvious in view of GenBank Accession No. AC006538 in combination with Kimmelman et al. and the '188 patent. Finally, claim 16 has been rejected under Section 103 (a) as allegedly *prima facie* obvious in view of GenBank Accession No. AC006538 in combination with Kimmelman et al. and the '809 and '703 patents. These rejections are traversed for the reasons set forth below.

In all of the above rejections, the Office relies principally on GenBank Accession No. AC006538 for its teaching of a 177,540 base pair nucleotide sequence, which comprises a 597 base pair nucleotide sequence, which is the subject of the present invention. The GenBank reference does not teach or suggest a recombinant expression vector consisting essentially of an open reading frame operably linked to one or more regulatory elements, wherein the open reading frame encodes the polypeptide of SEQ ID NO: 5, such as the nucleotide sequence of SEQ ID NO: 4, as claimed in instant claims 1 and 2, respectfully. In the absence of such a teaching or suggestion, the instantly rejected claims cannot be said to be obvious in view of the GenBank reference. In this regard, none of the secondary references cures the deficiencies of the GenBank reference. Therefore, the obviousness rejections cannot stand and should be withdrawn.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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